Prevalence of antidepressant-induced sexual dysfunction among psychiatric outpatients attending a tertiary care hospital

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ABSTRACT

الأهداف: لقياس انتشار الخلل الوظيفي الجنسي في مرضى العيادات الخارجية للأمراض النفسية الذين عولجوا بالفلوكستين أو الباروكستين أو الفينلافاكسين أو الميرتازابين.

المنهجية: أجريت دراسة مقطعية بأثر رجعي في مستشفى جامعة السلطان قابوس، مسقط ، عمان. دعينا جميع المرضى فوق سن 18 عام للمشاركة في الدراسة، الذين حضروا العيادة النفسية واستخدموا كلا من فلوكستين، باروكستين ، فينلافاكسين أو ميرتازابين لمختلف المؤشرات. تم تصميم ورقة لجمع البيانات لتوثيق الخصائص الديموغرافية للمرضى والتشخيص النفسي ونوع وجرعة ومدة العلاج المضاد للاكتئاب. تم استخدام جزء من الآثار الجانبية الجنسية من مقياس التأثير الجانبي لTSES لتقييم وجود خلل وظيفي جنسي.

النتائج: اشتملت الدراسة على 137 مريضا (ذكر: 51%، أنثى: 49%) في الدراسة. كان متوسط العمر للمشاركين 38 عامًا (المدى: 19-72 عامًا). وكان عدد المرضى لكل مضادات الاكتئاب على النحو التالي: باروكستين (52 مريضًا) ، فلوكستين (36 مريضًا) ، ميرتازابين (36 مريضًا) وفينلافاكسين (17 مريضًا). وكان متوسط مدة استخدام مضادات الاكتئاب 17 سنوات. كان معدل انتشار العجز الجنسي 39%. كان الباروكستين هو أكثر مضادات الاكتئاب شيوعًا المرتبطة بالاختلال الوظيفي الجنسي خاصةً بسبب انخفاض الرغبة الجنسية (59.6%) وتأخر القذف (34.4%). في المقابل، كان الميرتازابين هو الأقل بين مضادات الاكتئاب التي تسبب اختلال وظيفي جنسي.

الخلاصة: إن الخلل الجنسي شائع بين المرضى الذين عولجوا بمضادات الاكتئاب وخاصة مثبطات امتصاص السيروتونين الانتقائية (SSRIs). يمكن أن تؤدي معالجة هذه الآثار الجانبية المبكرة في العلاج إلى تحسين الامتثال للعلاج ومنع الانتكاسات

Objectives: To measure the prevalence of sexual dysfunction in psychiatric outpatients treated with fluoxetine, paroxetine, venlafaxine or mirtazapine.

Methods: This is a retrospective cross-sectional study conducted in Sultan Qaboos University Hospital, Muscat, Oman. All patients above 18 years of age, attending psychiatric clinic and taking fluoxetine, paroxetiene, venlafaxine or mirtazapine for various indications were invited to participate in the study. A data collection sheet was designed to document the patients' demographic features, psychiatric diagnosis, type, dose and duration of antidepressant treatment. Sexual side effects' part of Toronto Side Effect Scale (TSES) was used to assess the presence of sexual dysfunction.

Results: A total of 137 patients (Male: 51%, Female: 49%) were included in the study. The mean age for the participants was 38 years (range: 19-72 years).The number of patients for each antidepressant was as follows: paroxetine (52 patients), fluoxetine (36), mirtazapine (36 patients) and venlafaxine (17 patients). The average duration of the antidepressant use was 3.9 years. The overall prevalence of sexual dysfunction was 39%. Paroxetine was the most common antidepressant associated with sexual dysfunction especially for decreased libido (59.6%) and delayed ejaculation (34.4%). In contrary, mirtazapine was the lowest among antidepressants to cause sexual dysfunction.

Conclusion: Sexual dysfunction is common among patients treated with antidepressants particularly selective serotonin reuptake inhibitors (SSRIs). Addressing this side effects early in treatment can improve compliance to treatment and prevent relapse.

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Depression is one of the most common morbidities worldwide.[1] People with depression can experience limitations in their daily activities.[1] In 2017, major depressive disorder was considered as the third most common morbidity worldwide.[2] The use of antidepressants reduces the rates of morbidity and mortality associated with depression.[3] Several side effects have been linked to the use of antidepressants.[4] One of the most common side effects of antidepressants is sexual dysfunction.[5-7] Additionally, sexual dysfunction has been noted to be related to other risk factors including depression itself, other psychosocial factors, general medical illness, psychiatric disorders and some other medications.[4,8]

Patients experiencing antidepressant-induced sexual side effects usually under-report their symptoms.[9–12] Sexual dysfunction has various clinical manifestations and may present differently between males and females. In males, it presents as a decreased libido, difficulty in sustaining erection, anorgasmia, and delayed ejaculation.[7,12–14] In females, it presents as a decrease in sexual desire, impaired arousal and lubrication, and delayed orgasm.[10] Worsham et al[7](2018) reported that 32% of European patients taking antidepressants experience sexual dysfunction side effects. In another study (Balon 1993),[15] 43% of participants expressed having at least one sexual dysfunction symptom after taking antidepressants.In a multicentre descriptive study involving 344 patients, it was found that 61% of males and 52% of females reported having sexual dysfunction side effects.[16] Sexual dysfunction can affect the patient's quality of life and reduce their compliance to taking the antidepressant treatment.[7,12,14,17,18]

The risk of experiencing symptoms of sexual dysfunction following antidepressant treatment varies between the different classes of antidepressants and, more specifically, among antidepressants in the same class. Selective serotonin reuptake inhibitors (SSRIs), especially paroxetine, clomipramine and venlafaxine, are the most common antidepressants known to cause sexual dysfunction.[12,13,19,20]

This study aimed to examine the prevalence of sexual side effects among patients taking antidepressants attending the psychiatry clinic at Sultan Qaboos University Hospital; correlate the onset of antidepressant-induced sexual dysfunction with the patients' age, gender, diagnosis, duration of treatment and type of antidepressant used; indicate the rate of antidepressant-induced sexual dysfunction from four antidepressants commonly prescribed in Oman; and will set a platform for future studies examining specific side effects.

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Methods. This was a cross-sectional study conducted in the psychiatry clinic at Sultan Qaboos University Hospital (SQUH). All patients above 18 years of age attending the clinic from October 2017 to April 2018 were checked for their eligibility to participate in this study. All patients with a documented mental health disorder who were taking antidepressant medications and were being treated in the outpatient clinic within the dates specified were included. The antidepressants which were focused on in this study were: fluoxetine, paroxetine, venlafaxine and mirtazapine.

Ethical approval was obtained from the Medical Research and Ethics Committee (MREC) at Sultan Qaboos University and the study adhered to the Declaration of Helsinki (1964), which sets the standards for medical research on human subjects. A written consent from all participants was obtained after the study was explained to them. Patients were selected using systematic random sampling, and every third patient who attended the psychiatry clinic was invited to participate in the study. A psychiatric nurse invited the patients to participate in this study, explained the aims of the study, obtained the patient's consent and distributed the questionnaires. For illiterate patients, the information was collected by the nurse following

Table 1 - Patients' demographic characteristics.

Factor	n (%)
Age (years)	
18-40	89 (65.0)
41-60	37 (27.0)
>60	11 (8.0)
Sex	
Female	71 (51.0)
Male	66 (49.0)
Marital status	
Single	37 (27.0)
Married	93 (67.8)
Other	7 (5.1)
Diagnosis	
Depression	62 (45.0)
Anxiety disorders	49 (36.0)
Obsessive Compulsive Disorder	21 (15.3)
Other	5 (3.7)

Table 2 - Antidepressants usage, average doses and mean duration of use for the participants in this study.

Antidepressant	n	Average dose in mg (SD)	Mean duration of use in years (SD)
Paroxetine	52	22.3 (8.4)	5.1 (3.2)
Fluoxetine	36	25.5 (9.0)	2.7 (8.1)
Mirtazapine	32	20.4 (9.3)	3.3 (3.9)
Venlafaxine	17	94.8 (49.8)	4.5 (0.7)

Table 3 - Comparison of the percentages of decreased libido, increased libido and anorgasmia between the male and female participants in this study.

Symptoms	Male	Female	*P*-value *
	n (%)		
Increased libido	39 (59.0)	27 (38.0)	0.001
Decreased libido	46 (69.6)	38 (53.5)	0.265
Anorgasmia	45 (68.1)	37 (52.1)	0.054

*Pearson chi-square test was used to test the relationship between the 2 variables and the differences was considered statistically significant if the *p*-value <0.05

a verbal explanation of all of the questions. Medical records were then used to verify the information given by the participants. Sample size was calculated with the help of sample calculating website (www.surveysystem.com/sscalc.htm), taking into consideration the total number of patients attending SQUH psychiatric outpatient clinic, with a confidence interval (CI) of 95%. A data collection sheet was used to collect the patients' demographics and to record the patient's diagnosis, duration of treatment, antidepressant used and presence of psychiatric or medical comorbidities.

The patients' mental health disorder diagnosis was based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). Patients were excluded if they declined to sign a written consent form and when their clinical presentation was not consistent with DSM-5 criteria for any mental health disorder.

Assessment tool. The Toronto Side Effects Scale (TSES) was used to measure the side effects of the antidepressants included in the study. The TSES is a clinician-administered antidepressant side effects scale developed by Vanerdkooy and his colleagues in 2002. This scale rates the frequency and severity of 32 side effects from 3 major areas which are affected by antidepressants' side effects: central nervous system, gastrointestinal system and sexual functions. This study concentrated only on the sexual side effects portion of the scale. The scale was a useful tool to measure antidepressant side effects.[21]

Data management. Data analysis was done using the Statistical Package for the Social Sciences (SPSS) version 22 (IBM Corp., Armonk, NY, USA). Categorized variables were described as percentages with confidence intervals (CIs). Continuous variables were presented as means with standard deviation (SD) or medians with inter-quartile range. To assess the relationships between the variables a univariate analysis Chi-square test, the t-test and analysis of variance (ANOVA) were used.

Results. The total number of patients who participated in the study was 137 (male: 49%, female: 51%). The average age of the participants was 38-years-old (range: 19-72 years). Most of the participants were married (67.8%), non-smokers (96%), did not drink alcohol (99%) and had no medical comorbidity (93.5%).

Major depressive disorder was the most common diagnosis among the participants (45%), followed by anxiety disorders (36%) and obsessive compulsive disorder (15.3%). **Table 1** summarizes the patient demographic data and the frequency of the various diagnoses.

Among the participants of this study, 38.0% were taking paroxetine, 26.3% fluoxetine, while 23.4% used mirtazapine and 12.4% took venlafaxine. The mean duration of antidepressant use and the average dosage can be found in **Table 2**.

The overall prevalence of sexual dysfunction among the participants of this study was 39.1%, with more than third of the participants experienced at least one sexual side effect from the antidepressants. Among the male participants, delayed ejaculation, premature ejaculation and erectile dysfunction were reported in 29.0%, 55.6% and 40.0% respectively. Decreased libido was reported by 45.0% of all participants, while 40.0% experienced anorgasmia following the use of antidepressants. Male participants reported increased and decreased libido, as well as anorgasmia, more frequently than the female participants, although the difference was only noted to be statistically significant ($p<0.05$) - using univariate analysis Chi square test - for increased libido. **Table 3** compares the percentages of decreased libido, increased libido and anorgasmia between the male and female participants in this study.

Using univariate analysis Chi square test, there were no statistical differences in the onset of sexual dysfunction between the age groups. Of the participants using antidepressant therapy for more than one year,

Table 4 - Rate (w%) of sexual dysfunction among participants per antidepressant.

	Fluoxetine (%)	Mirtazapine (%)	Paroxetine (%)	Venlafaxine (%)	p-value*
Decreased libido	(29.4)	(28.0)	(59.6)	(47.0)	0.189
Increased libido	(26.4)	(21.8)	(25.0)	(29.4)	0.996
Premature ejaculation	(33.3)	(46.1)	(62.0)	(77.0)	0.466
Delayed ejaculation	(22.2)	(30.7)	(34.4)	(22.2)	0.909
Anorgasmia	(35.2)	(28.1)	(48.0)	(52.9)	0.240
Erectile dysfunction	(27.7)	(38.4)	(44.8)	(44.4)	0.635

*Pearson chi-square test was used to test the relationship between the 2 variables and the differences was considered statistically significant if the *p*-value <0.05

42.6% of them experienced adverse sexual side effects. In contrast, only 23.6% of participants reported adverse sexual side effects after using antidepressants for less than a year.

Of the 4 antidepressants observed in this study, paroxetine was found to cause the highest rate of decreased libido (59.60%) and delayed ejaculation (34.44%) mong all participants. Venlafaxine and paroxetine were associated with erectile dysfunction, anorgasmia and premature ejaculation more frequently than mirtazapine and fluoxetine. With regards to the onset of the sexual dysfunction between all of the antidepressants, there was no statistically significant difference. **Table 4** shows the rate of each sexual side effect for each antidepressant.

Discussion. Due to several socio-cultural factors, studies relating to sexual health are uncommon in Oman. This study was conducted in a tertiary care hospital in Muscat, which receives referrals from all areas of Oman. Therefore, this study's population should represent people from all of the Omani governates. The antidepressants included in this study were selected based on findings from a pharmacy audit, indicating that these were the four most commonly prescribed antidepressants in the psychiatry clinic of SQUH. As part of the patient screening, inquiries about the sexual functions of all participants were made to ensure that the sexual dysfunction was due to the antidepressant treatment.

In the present study, more than a third of participants (39.1%) reported to have at least one sexual dynsfunction symptom following the use of antidepressants. This finding is consistent with many previous studies which have found that a significant number of patients complained of sexual dysfunction following antidepressant treatment.[22,23] One study, by Lee et al (2010)[23] found that 46.5% of patients attending a metal health clinic suffered from sexual dysfunction after taking antidepressant. Montejo et al[12] examined 1022 patients in multiple centres around Spain and found that more than half of the participants (59.1%) experienced sexual dysfunction after being prescribed antidepressants.

This study found that the rate and type of sexual dysfunction varied depending on the antidepressant. For example; paroxetine was associated with a higher incidence of decreased libido and delayed ejaculation as compared to other antidepressants. Patients taking mirtazapine and fluoxetine reported less sexual dysfunction than those on paroxetine and venlafaxine. These findings replicate the results of other similar studies, which showed that paroxetine was linked to a higher frequency of sexual dysfunction.[12,23,24] Paroxetine causes higher rates of sexual dysfunction due to its mechanism of action, as paroxetine blocks D2-receptors which have been found to be directly involved in the sexual functions of animals. Moreover, it inhibits the synthesis of nitric oxide which is essential for erections.[25,26]

The reason that mirtazapine is less likely to cause sexual dysfunction is also related to its unique mechanism of action. Mirtazapine blocks 5-HT2 and 5-HT3, which have been associated with fewer sexual side effects and the ability to promote orgasm.[12]

Sexual side effects following antidepressant therapy usually appear in the early stages of the treatment. This is especially true for paroxetine, which often causes decreased libido and erectile dysfunction in the first month of therapy.[27] However, in this study patients who used antidepressant medication for more than one year experienced more sexual dysfunction than patients who used it for less than 1 year. This may be attributed to the fact that most patients who experience

sexual dysfunction discontinue their medication early in the treatment or switch to another medication less likely to cause sexual side effects. Moreover, it may be related to specific ethnic variations which can affect the pharmacokinetic nature of the antidepressants and results in a prolonged discrepancy between prescribing the antidepressant and the onset of the side effects.[28] However, this needs further exploration by future researches.

It is imperative to address the sexual side effects of antidepressants during patients' follow-up appointments. Several studies have shown that treatment non-compliance is common among patients who experience sexual dysfunction following antidepressant treatment.[24] This results in treatment failure and recurrence of depressive symptoms. Furthermore, sexual dysfunction after antidepressant therapy was found to have a direct negative impact on patient self-esteem and their quality of the life, and can also impact their relationship with a sexual partner.[29]

Limitations. The sample size for this study is relatively small when divided across the 4 antidepressants involved in this study. Moreover, some patients may under-report sexual side effects due to the sensitivity of this issue in the Arabic culture. This may affects the numbers representing the prevalence of sexual side effects when compared to other cultures.

Conclusions. Sexual side effects are common among patients who are being treated with antidepressant medications. Paroxetine and venlafaxine were found to be associated with an increased risk of sexual dysfunction as compared to fluoxetine and mirtazapine. Addressing patients' sexual dysfunctions early on in their treatment can improve patient compliance to treatment and prevent relapse.

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